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EXAMINER	
CANELLA, KAREN A	
ART UNIT	**PAPER NUMBER**
1642	

DATE MAILED: 03/25/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/852,547	SIRBASKU, DAVID A.	
	Examiner	Art Unit	
	Karen A Canella	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *1-15,17-20 and 66-90* is/are pending in the application.

4a) Of the above claim(s) *90* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *1-15,17-20 and 66-89* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on January 8, 2004 has been entered.

Claims 1, 2, 4-15, 17-20, 66-72, 75, 78 and 80 have been amended. Claims 16, 21-65 have been canceled. Claims 81-90 have been added. Claim 90, drawn to a non-elected invention, is withdrawn from consideration. Claims 1-15, 17-20 and 66-89 are under consideration.

Claims 1-6, 66, 67, 70, 73-76, 81 and 89 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is lacking an active method step wherein the outcome of method steps (a)-(c) is linked with the method objective of predicting susceptibility of a mammalian subject to the development or growth of a steroid hormone responsive cancer in a mucosal epithelial tissue as recited in the preamble. Claim 1 is also unclear in the recitation of section (c) which lacks a precise statement of how said "determination of step (b)" is further used to indicate "that an absence or deficiency indicates" insufficient immunoglobulin inhibitor.

Claim 2 is vague and indefinite because it is unclear if the obtaining a sample of at least one body fluid or secretion is in addition to the body fluid or secretion of step (a) of claim 1.

The metes and bound of what constitutes "substantial no free ferric ion" in claims 5 cannot be determined because the level at which the free ferric ion becomes "substantially no" free ferric ion in contrast to "no" free ferric ion are unclear.

Claim 5 recites testing said specimen for "cytotoxic effects". cytotoxic effects can be manifest by stasis, growth inhibition, apoptosis and necrosis. for purpose of examination, all alternatives will be considered.

Claim 7 is vague and indefinite in the recitation of section (c) which lacks a precise statement of how the assay results form step (a) and optionally from step (b) are to be "used" to

determine that the absence or deficiency of said receptor indicates loss of "immunoglobulin regulation of growth".

Claim 8 is vague and indefinite in the recitation of section (c) which lack a precise statement of how the assay results from step (a) and optionally step (b) are to be "used". Further the testing said poly-Ig receptor for in vitro activity is not linked with the method objective of detecting a mediator of immunoglobulin inhibitor of steroid hormone responsive cell growth.

Claim 9 lacks an active method step which relates the outcome of the final method step with the method objective as set forth in the preamble.

Claim 10 is vague and indefinite. the method recites "identifying a loss of heterozygosity or an allelic imbalance in a poly-Ig receptor gene". It is unclear how the identification of a loss of heterozygosity or an allelic imbalance related to the method objective of detecting a "variant poly-Ig receptor gene" as recited in the method pre-amble. Claim 10 is further vague and indefinite in the recitation of "matching said screened poly Ig receptor gene from said cancerous cell to a poly-Ig receptor gene form said non-cancerous cell". It is unclear what said "matching" entails.

Claim 11 is vague and indefinite as it lacks correlation between the final method step and method objective as recited in the preamble. further, it is unclear how said gene is to be "expressed" firstly, because this is not a method of recombinant expression and secondly, the method object states that this is a method of detecting a defective mediator. It flows logically from this that if the mediator has not yet been detected in a cell it can't be expressed in said cell.

Claim 12 is vague and indefinite, lacking a precise statement of how the assay results form step (a) are to be "used" to predict susceptibility of said subject to the devolvement of breast cancer.

Claim 13 is vague and indefinite, lacking a precise statement of how the assay results from step (a) and optionally from step (b) are to be "used" to determine increase susceptibility.

Claim 14 is vague and indefinite in the recitation of "normally steroid hormone responsive". It is unclear what this normality is in reference to. For purpose of examination, the claim will be read as "steroid hormone responsive normal mucosal epithelial cells".

Claim 14 is also vague and indefinite, lacking a precise statement of how the assay results from step (a) and the optional results from steps (b) are to be "used" to determine if said mucosal epithelial said have transformed.

Claim 15 is vague and indefinite. the method preamble states "a method to aid in detecting progression of a steroid hormone responsive malignant mucosal epithelial cell to a autonomous cancer cell". however, the active method steps require the testing and assaying of said "autonomous cancer cell". It is unclear how the testing of an autonomous cancer cell can aid in detecting progression to an autonomous cancer cell, as said method requires the testing of autonomous cancer cells in which the progression would already have occurred. further, the claim lacks a precise statement of how the assay results form step (a) and optionally from step (b) are to be "used" to met the method objective as recited in the preamble.

Claim 17 is vague and indefinite in the recitation of "using the results of said determinations and detections to aid in detecting or diagnosing cancer". The recitation of "using" is not a precise method step and does not describe any particular action. Claim 17 is also vague and indefinite the recitation of "said absence or diminution indicating the presence of a cancerous or precancerous lesion in said patient". It is unclear if "said absence or diminutions" refers to the absence or diminution of all of the first set of conditions listed or at least one. the method preamble indicates that "at least one of a first set of conditions is selected from the following". Thus, according to the method preamble only one absence or diminution need be detected. However, the claim also recites "an absence of one or more of said conditions indicating the absence of a cancerous or precancerous condition". The method appears to have conflicted directions. for instance the absence or diminution of a poly-Ig receptor can be detected, however, the same cells can exhibit heterozygosity for the Fcgamma receptor. Thus, said cells will fulfill the criteria of absence or diminution indicative of a cancerous or precancerous lesion, and also having the absence of one or more or said conditions "absence of heterozygosity" and therefore indicative of the absence of a cancerous or precancerous lesion.

Claim 18 is vague and indefinite, lacking a precise statement of how said determinations are to be "used" to met the method objective as recited in the preamble.

Claim 19 is vague and indefinite, lacking a precise statement of how the determinations from sections (b) and (c) are to be "used" to met the method objective as recited in the preamble.

Claim 20 is vague and indefinite, lacking a precise statement of how the detection form section (a) is "used" to "aid in treating cancer" as recited in the pre-amble. claim 20 is also vague and indefinite in the recitation of the relative term : high-affinity.

Claim 68 is vague and indefinite, lacking a precise statement of how said detection from step (a) and optionally from step (b) is to be used in the determination of the capability of the Fcgamma receptor to mediate immunoglobulin inhibition of steroid hormone responsive cell growth. further, it is unclear how the outcome of the final method step related to the method objective as recited in the preamble.

Claim 69 lack an active method step relating the outcome of the final active method step with the method objective of detecting a "defective mediator". It is noted that the claim relies on the variant Fcgamma receptor identified in claim 80. claim 80 contains the limitation that said variant receptor lacks or has reduced ability to mediate inhibition by IgG1. thus it is unclear how testing of the variant protein in claim 69, which is already known to lack ability to mediate steroid hormone inhibition, pertains to the detection of a "defective mediator" of immunoglobulin inhibition as recited in the preamble.

Claim 71 is vague and indefinite lacking a precise statement of how assay results from step (a) and optionally test results from step (b) are to be used to determine that the absence or deficiency of said receptor.

Claim 72 is vague and indefinite lacking a precise statement of how the determination of whether the Fcgamma receptor encoded by said gene has the property of being capable of mediating by IgG1 or IgG2.

Claims 73-76 fail to relate the limitations of "detecting a poly-Ig receptor in said mucosal epithelial cell", "detecting a Fcgamma receptor in said mucosal epithelial cell", "assessing the activity of said Fcgamma receptor" and "identifying an age range in said mammalian subject" with the method objective of claim 1 as recited in the preamble.

Claims 77 and 78 fail to link the outcome of the active method step with the method objective a recited in the preamble. It s unclear how the identification of a loss of heterozygosity in claim 80 relates to the method objective as recited in the preamble. It is noted that this method step is listed in the alternative to the remainder of the method steps. Further the metes and bounds of what constitutes "matching" said screened Fcgamma receptor genes cannot be determined as

matching can be construed to means both homologous as well as exact matching and no limitations are given for the metes and bounds of a homologous "match".

Claim 82 is vague and indefinite in the recitation of "comparatively lower level" without indication of what is being compared. further claim 82 is vague and infinite in the lack of precise statement of how the comparative results of step (c) are to be used to predict susceptibility.

It is unclear how claim 83 further limits claim 82. Claim 82 recites the method objective of predicting susceptibility to the development of breast cancer. claim 83 embodies the method of claim 82 wherein the comparatively lower level indicates increased susceptibility to mutagenesis or carcinogenesis. the limitation of increased susceptibility to carcinogenesis is inherent in the method of claim 82 and thus fails to further limit claim 82.

Claim 84 and 85 fail to correlate the outcome of the active method step with the method objective as recited in claim 82.

Claim 89 is vague and indefinite because it is unclear if "obtaining a serum or plasma sample from said subject" is separate from obtaining at least one specimen of body fluid or secretion form said subject. If it is applicants intent to further limit the identity of said body fluid or secretion, then claim 89 can be states, the method of claim 1 wherein at least one specimen of body fluid or secretion obtained from said subject is serum or plasma.

Claims 18, 70, 82-85are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. .

Claim 18 recites "mucosal epithelial; tissues which is in a forma that is active for inhibiting steroid hormone responsive cell proliferation".

Claim 70 "combination thereof". Claim 70 embodies the method of claim 1 wherein said immunoglobulin receptor comprises dimeric/polymeric, IgA, polymeric IgM, IgG1, or IgG2, or any combination thereof.

The specification states on page 10, [0018] that for "purpose of this disclosure, the term "immunoglobulin inhibitor" refers to a secretory immunoglobulin, preferably on of the secretory immunoglobulins IgA, IgM and Ig1 that is active for inhibiting proliferation of a steroid hormone responsive cancer cell. This statement does not provide support for the inclusion of "form that is active for inhibiting steroid hormone responsive cancer cells" or "combination thereof". The specification does not contemplate a chimeric secretory immunoglobulin comprising a combination of secretory immunoglobulins.

Claim 20 has the newly incorporated limitation of having a greater E2 binding affinity than that of ERalpha or ERbeta. support for this limitation was not found in the specification as filed. applicant is reminded to provide page and line numbers indicated where support in the specification can be found for amendments and new claims.

Claim 82 "age range during which DNA synthesis in breast tissue is expected to be increased compared to another age range". the specification states on page 172 [0572] that "human female breast cancer incidence rates increase dramatically after age 50 and now approach one in eight by age 75. the existing data suggests that the casual mutations most likely occur at earlier ages. however, breast milk secretions decrease dramatically after menopause. Perimenopausal and postmenopausal woman may have an unrecognized "window" of increased vulnerability because the activity of the secretory immune system decreases with the approach of mid-life". This does not provide support for the limitation "age range during which DNA synthesis in breast tissue is expected to be increased".

Claim 17 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention..

Claim 17 is inoperative for the reason stated in the rejection under 112, 2nd above, namely: the method preamble indicates that "at least one of a first set of conditions is selected from the following". thus, according to the method preamble only one absence or diminution need be detected. however, the claim also recites "an absence of one or more of said conditions indicating the absence of a cancerous or precancerous condition". The method appears to have

conflicted directions. For instance the absence or diminution of a poly-Ig receptor can be detected, however, the same cells can exhibit heterozygosity for the Fcgamma receptor. Thus, said cells will fulfill the criteria of absence or diminution indicative of a cancerous or precancerous lesion, and also having the absence of one or more or said conditions "absence of heterozygosity" and therefore indicative of the absence of a cancerous or precancerous lesion. Given the conflicted directions within the claim, one of skill in the art would be subject to undue experimentation in order to practice the claimed method.

Claims 1-6, claim 17 in part, 18 in part, 19 in part, 66, 67, 70, 73-76 and 81-86 and 89 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention..

Claims 1-6, claim 17 in part, 18 in part, 19 in part, 66, 67, 70, 73-76 and 81-86 and 89 are rejected under 112, first lack of enablement for quantitating or detecting an immunoglobulin inhibitor of steroid hormone responsive cell growth in a specimen of body fluid or secretion. the specification states on page 10, [0018] that for "purpose of this disclosure, the term "immunoglobulin inhibitor" refers to a secretory immunoglobulin, preferably on of the secretory immunoglobulins IgA, IgM and Ig1 that is active for inhibiting proliferation of a steroid hormone responsive cancer cell. The specification bases the instant claims on the premise that measurement of said secretory immunoglobulins would then be diagnostic for inhibition of steroid responsive cell growth and that decreased levels of said immunoglobulins would then be indicative of decreased inhibition of said cell growth. The specification teaches that the secretory immunoglobulin system decreases activity with age. this is a general teaching dependent upon the averaging of multiple measurements of secretory immunoglobulins over a period of time encompassing years. However, it is known in the art that levels of IgA, the major secretory immunoglobulin, vary as a function of time of day, as well as within a year, and large variations between healthy subjects is documented (Garde et al, Clinical Chemistry, 2000, Vol. 46, pp. 551-559, cited in a previous action). The art also teaches that levels of secretory IgA is hormonally regulated in women and thus variable over the curse of a menstrual cycle (Gomez et

al, Amer J Reproduc Immunol, 1993, Vol. 29, pp. 219-223, cited in a previous action). It would be reasonable to conclude that the level of the other types of secretory immunoglobulins would also vary as a function of the exposure of an individual to exogenous antigens or substances provoking an immune reaction. Thus, it would be reasonable to conclude that the measurement of secretory immunoglobulins in a single sample would not be representative of the average level of secretory immunoglobulins present within an individual during the course of a year or more. Given that the art teaches that the level of IgA, the major secretory immunoglobulin, varies both positively and negatively with time in a healthy individual and also varies between individual subjects and thus supports the conclusion that the level of other sercretory immunglobulins also vary with time by both increasing and decreasing; and given the lack of teachings in the specification regarding ranges or levels of secretory immunoglobulins that were indicative of normal individual versus individuals having a steroid hormone responsive cancer, one of skill in the art would be subject to undue experimentation in order to make and use the claimed methods relying on correlating the levels of secretory immunoglobulins with the presence or susceptibility to steroid hormone responsive cancer.

Claims 7, 8, 9, 10, 11, 12, 13, 14, 15, 17, 18, 19, 68, 69, 72, 79 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods reliant upon the measurement of the ability of the poly-Ig receptor to mediate steroid hormone responsive cell growth in a specimen of mucosal epithelial cells, wherein cell specimen is a cultured cell line, does not reasonably provide enablement for methods reliant upon the measurement of the ability of the poly-Ig receptor to mediate steroid hormone responsive cell growth in a specimen of mucosal epithelial cells, wherein the specimen is taken from a patient. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims..

Claims 7, 8, 9, 10, 11, 12, 13, 14, 15, 17 in part, 18 in part, 19 in part, 68, 69, 72, 79 are drawn to method claims reliant upon the measurement of mediation of inhibition of steroid hormone responsive cell growth. the specification provides guidance for how to measure immunoglobulin inhibition of steroid hormone responsive cell growth using cultured cell lines,

wherein the measurement of growth inhibition requires the measurement of significant differences in "cell population doublings". Claims 11, , 12, , 13, 17, 18, 19 and 69 contain specific embodiments relating to obtaining mucosal epithelial cells from a patient. Claims 7-10, 14, 15, 68, 72 and 79 read on generic mucosal epithelial cells and therefore encompass methods comprising cultured mucosal epithelial cell lines and samples of mucosal epithelial cells taken from patients. It is reasonable to conclude that cell taken from patient samples would be required to grow to the extent that "cell populations doublings" occur to a significant degree in order than statistically significant numeric value for cell inhibition can be obtained. It is noted that applicant argued against the examiners previous rejection of the word "significant" under 112, second paragraph by stating that the specification defines "significant" as statistically significant. It is well known in the art that primary cells obtained from patients do not grown well in culture (Freshney, Culture of Animal Cells, 1994, page 351, second column, third full paragraph), most of the cells, if nor all of the cells not being able to propagate. Thus, it is unlikely that a sample of mucosal epithelial cells taken from a patients will persists long enough to provide a statistically significant number of population doublings on which to measure the loss of immunoglobulin regulation of growth of said cells. Given the state of the art with respect to the inability of primary cells to grow in culture and the lack of teachings in the specification which address or remedy said problem, one of skill in the art would be subject to undue experimentation in order to use the claimed methods to detect loss of immunoglobulin regulation of cell growth, or defective or variant poly-Ig receptors.

Claims 8, 9, 10, 11, 13, 14, 17, 19, 67, 68, 69, 71 , 72, 80 and 88 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. .

Claims 8, 9, 10, 11, 13, 14, 17, 19, 67, 68, 69, 71 , 72, 80 and 88 contain the limitations of "mediator of immunoglobulin inhibition of steroid hormone responsive cell growth". "defective mediator of immunoglobulin inhibition of steroid hormone responsive cell growth", "a ply-Ig receptor" "an Fc receptor" , a "variant Fcgamma receptor", and "altered domain in said

poly Ig receptor". The specification states on page 11[0022] that "certain other embodiments of the invention provide a method of detecting a mediator of immunoglobulin inhibition of steroid hormone responsive cell growth that includes detecting a poly-Ig receptor". Thus, claims drawn to an immunoglobulin inhibitor of cell growth comprises a genus of inhibitors which include a poly-Ig receptor but is not limited only to poly-Ig receptors. further, given that the claim limitations require the determination of mediation of inhibition of steroid hormone cell growth , it in concluded that claims drawn to poly-Ig receptors and Fc receptors encompass defective and variant receptors which differ in amino acid sequence and function from the wild type receptors. Claims 10, , 11, , 69, 80 are specifically drawn to rely on the identity of variant poly-Ig and Fcgamma receptors and genes. The claims are thus drawn to a genus of molecules encompassing mutant, truncated and otherwise variant poly-Ig or Fc receptor proteins. The claims do not limit the "defect" in terms of specific structural or specific functional characteristics., thus it is not possible to determine if a given protein is member of the claimed genus The specification does not teach a representative number of defective poly-Ig receptors or defective Fc receptors that would be representative of the claimed genus. Because the genuses are highly variant, reliance on a description of the poly-Ig receptor or the Fcgamma receptor is insufficient to anticipate the claimed genus.

Claims 10, 11, 69, and 80 are reliant upon the identity of poly-Ig receptor alleles, poly Ig receptors having altered domains, genetically defective poly Ig receptor genes, alleles of Fc receptor genes and genetically defective Fc receptor genes. The specification provides no teachings regarding DNA sequence or the protein encoded therefrom for any of the aforesaid variants or alleles of the poly Ig receptor or the Fc receptor. Although drawn to DNA arts, the findings in University of California v. Eli Lilly and Co., 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997) and Enzo Biochem, Inc. V. Gen-Probe Inc. are relevant to the instant claims. The Federal Circuit addressed the application of the written description requirement to DNA-related inventions in University of California v. Eli Lilly and Co., 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997). The court stated that "[a] written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." Id. At 1567, 43 USPQ2d at 1405. The court also stated that a generic

statement such as "vertebrate insulin cDNA" or "mammalian insulin cDNA" without more, is not an adequate written description of the genus because it does not distinguish the genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. A definition by function, as we have previously indicated, does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is. Id. At 1568, 43 USPQ2d at 1406. The court concluded that "naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material." Id. Finally, the court addressed the manner by which a genus of cDNAs might be described. "A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus." Id. The Federal Circuit has recently clarified that a DNA molecule can be adequately described without disclosing its complete structure. See Enzo Biochem, Inc. V. Gen-Probe Inc., 296 F.3d 1316, 63 USPQ2d 1609 (Fed. Cir. 2002). The Enzo court adopted the standard that "the written description requirement can be met by 'show[ing] that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics ....i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics. " Id. At 1324, 63 USPQ2d at 1613 (emphasis omitted, bracketed material in original).

The inventions at issue in Lilly and Enzo were DNA constructs per se, the holdings of those cases are also applicable to claims such as those at issue here. A disclosure that does not adequately describe a product itself logically cannot adequately describe a method of using that product.

Thus, the instant specification may provide an adequate written description of the immunoglobuin inhibitor which demonstrates binding, per Lilly by structurally describing a representative number of immunoglobulin inhibitors that are capable of binding to a specific

poly Ig or Fc receptor, and can be reversible inhibited by binding of a specific steroid hormone to a specific steroid hormone receptor and or by describing "structural features common to the members of the genus, which features constitute a substantial portion of the genus.". Alternatively, per Enzo, the specification can show that the claimed invention is complete "by disclosure of sufficiently detailed, relevant identifying characteristics, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics."

In this case, the specification does not describe the immunoglobulin inhibitor , or the steroid hormone/steroid hormone receptor to practice the methods of the instant invention in a manner that satisfies either the Lilly or Enzo standards. The specification does not provide the complete or partial structure or physical or chemical structure of the immunoglobulin inhibitor or steroid hormone receptor, nor any physical or chemical characteristics of the immunoglobulin inhibitors and steroid hormone receptor coupled with a known or disclosed correlation between structure and function. Thus, it is concluded that the specification does not provide a description of the disclosed immunoglobulin inhibitors or steroid/steroid hormone receptor that would satisfy the standard set out in Enzo.

The specification also fails to describe the immunoglobulin inhibitor and steroid hormone/ steroid hormone receptor by the test set out in Lilly. The specification contemplates only a "immunoglobulin inhibitor" and a "steroid hormone/steroid hormone receptor". Therefore, it necessarily fails to describe a "representative number" of such species. In addition, the specification also does not describe "structural features common to the members of the genus, which features constitute a substantial portion of the genus."

Thus, the specification does not provide an adequate written description of the immunoglobulin inhibitors, poly Ig receptors, Fc receptors, steroid hormone receptors required for the practice of the instant method claims. Since the specification fails to adequately describe disclosed immunoglobulin inhibitor, "a" poly Ig receptor or "a" Fc receptor and steroid hormone/steroid hormone receptor, it also fails to adequately describe the method reliant upon said products.

Thus it is concluded that the disclosure of a immunoglobulin inhibitors and a steroid hormone/ steroid hormone receptor does not describe the claimed genus, because said genus

encompasses members with structural and functional attributes which are unknown. Accordingly, one of skill in the art would conclude that applicant was not in possession of the claimed genus.

Regarding alleles and defective gene sequences, the specification does not identify said variant gene sequences. The general knowledge and skill in the art concerning alleles is that the structure of one allele is not representative of other unknown alleles. The same can be said of mutant genes, such as those encoding "defective" poly Ig receptor and defective Fc receptors. thus, the nature of both alleles and defective Fc receptors and defective poly Ig receptors is that they are variant structures and the in the present state of the art, the structure of one does not provide guidance for the structure of other s. The common attributes of the genus are not described. One of skill in the art would conclude that applicant was not in possession of the claimed genus because a the known genes encoding the poly Ig receptor and the Fc receptor are not representative of the variants of the claimed genus. One of skill in the art would conclude that applicant was not in possession of the claimed genus.

Claims 20 and 77-79 are method claims reliant on the detection of a "high affinity estrogen binding activity". the specification does not provide any structural characterization for said "high affinity estrogen binding activity". It is noted that said "high affinity estrogen binding activity" includes a genus which is highly variant encompassing not only estrogen receptors, but drug molecules which bind estrogen. Further, to repeat the argument stated above, that "[a] written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." Id. At 1567, 43 USPQ2d at 1405. The court also stated that a generic statement such as "vertebrate insulin cDNA" or "mammalian insulin cDNA" without more, is not an adequate written description of the genus because it does not distinguish the genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. A definition by function, as we have previously indicated, does not suffice to define the genus because it is only an indication of what the gene does, rather

than what it is. Id. At 1568, 43 USPQ2d at 1406. The court concluded that "naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material." . Accordingly to this analysis, the recitation of a "high affinity estrogen binding activity" is clearly what the product does, but not what it is.

Claims 20, 78 and 79 are rejected under 35 U.S.C. 102(b) as being anticipated by Barton et al (WO 99/05171). Claim 20 is drawn to a method to "aid" in treating cancer of a mucosal epithelial tissue comprising detecting in a population of cancer cells a high affinity estrogen binding activity having a greater E2 binding affinity than that of ERalpha or ERbeta. Claim 78 embodies the method of claim 20 comprising identifying antagonists of said high-affinity estrogen receptor. Claim 79 embodies the method of claim 78 wherein said antagonist is tamoixifen.

Barton et al teach a method of detecting the ERbeta"c" receptor (pages 28-30, section E, "Determining tissue localization of ERbeta"c" or its isoforms by nucleic acid hybridization"). It is noted that claim 20 is rejected under 112, second for lacking a nexus between the final active method step and the method objective as recited in the preamble. Barton et al teach methods of identifying agent which modulate the interaction of ERbeta"c" with estrogens (page 10, lines 25-27, page 11, lines 19-23 and claim 17), wherein one of said agents was tamoxifen (page 16, lines 20-24). Barton et al teach that ERbeta"c" is not the ERbeta sequence as published previously (page 10, lines 1-2). Barton et al teach that the ER-beta3 isoform of ERbeta"c" has a much higher affinity for E2 than ERalpha. Barton et al do not specifically compare the E2 affinity of ER-beta3 with the prior art ERbeta sequence. However, the claimed estrogen-binding activity appears to be the same as the prior art ERbeta"C" receptor and isoforms thereof, absent a showing of unobvious differences. The office does not have the facilities and resources to provide the factual evidence needed in order to establish that the product of the prior art does not possess the same material, structural and functional characteristics of the claimed product. In the absence of evidence to the contrary, the burden is on the applicant to prove that the claimed product is different from those taught by the prior art and to establish patentable differences. See In re Best 562F.2d 1252, 195 USPQ 430 (CCPA 1977) and Ex parte Gray 10 USPQ 2d 1922 (PTO Bd. Pat. App. & Int. 1989).....

All other rejections and objections as set forth in the previous Office action are withdrawn in light of applicants amendments.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Karen A Canella whose telephone number is (571)272-0828. The examiner can normally be reached on 10 a.m. to 9 p.m. M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler can be reached on (571)272-0871. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

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03/22/04

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